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(54) Title: SUBSTANTIALLY ANHYDROUS COMPLEXES OF PVP and H_2O_2

(57) Abstract

What is provided herein are substantially anhydrous complexes of PVP and H_2O_2 in molar ratios of between about 2:1 and 1:1, respectively, which corresponds to between about 13 % and about 23 % by weight H_2O_2. The complexes of the invention are substantially uniform, free-flowing, fine white powders. The complexes herein are prepared by reacting PVP and H_2O_2 in substantially the molar ratio predetermined for the complex. In one suitable process for preparing such complexes the reaction is carried out between the reactants in an anhydrous organic solvent such as ethyl acetate. A method is provided herein for reducing the microbial content of surfaces which comprises contacting said surface with a microbiocidal amount of said free-flowing, substantially anhydrous complex of PVP and H_2O_2.

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SUBSTANTIALLY ANHYDROUS COMPLEXES OF PVP AND H_2O_2

This invention relates to substantially anhydrous complexes of polyvinylpyrrolidone (PVP) and hydrogen peroxide (H_2O_2) which are, free-flowing, uniform, fine white powders containing a predetermined amount of H_2O_2 therein.

Stabilized H_2O_2 compositions have found wide utility in commercial and industrial applications, e.g. as disinfectants, sterilization agents, as bleaching materials, washing concentrates, etchants, in cosmetic preparations, as clarification agents for alcoholic and fermented beverages, and as a catalyst in polymerizations requiring a free radical source. In biological applications which require a disinfectant or sterilization agent, such H_2O_2 compositions require release of an effective amount of oxygen at a controlled rate without storage decomposition caused by interaction with organic matter, light and/or heat.

Shiraeff, in U.S. Patents 3,376,110 and 3,480,557, discloses a solid, stabilized hydrogen peroxide composition of hydrogen peroxide and a polymeric N-vinyl heterocyclic compound prepared in an aqueous solution of the components. These compositions generally were prepared by mixing various weights of PVP and aqueous H_2O_2, and evaporating the solution to dryness. The Shiraeff composition, which was believed to be a solid, dry complex, was described as not necessarily anhydrous due to the hydrophilic nature of the PVP and the water present in the reaction solution. Shiraeff further stated that such amounts of water could be tolerated, however, if it did not affect the solid dry characteristics of the complexes. The H_2O_2 content of the composition was given as being at least 2%, and pref rably 4.5 to 70% by weight. Prolonged

drying to remove wat r from such compositions, however, resulted in loss of H_2O_2 forming a brittle, transparent, gummy, amorphous product. In U.S. 3,480,557, the aqueous PVP-H_2O_2 complexes, upon heating to dryness, produced hard, brittle chips which had a variable H_2O_2 content ranging from about 3.20 to 18.07% by weight, depending upon the drying times.

In accordance with the invention, substantially anhydrous PVP-H_2O_2 complexes are provided having a predetermined molar ratio of PVP to H_2O_2 ranging from between about 2:1 to about 1:1, corresponding to a H_2O_2 content of about 13% to about 23%. The substantially anhydrous PVP-H_2O_2 complexes are prepared by reaction of PVP and H_2O_2 in a substantially anhydrous organic solvent and are obtained by filtration of the suspension as a uniform, free-flowing, fine white powder.

The PVP polymeric starting material used in the present invention is available commercially as a solid of varying molecular weight, water solubility and water content. A typical PVP polymer is water soluble PVP-K30 (GAF Corp.) which contains less than 5% water. Other PVP polymers of different molecular weight, water solubility and water content also may be used, as for example, K-90 and K-120; Polyclar AT; Crospovidone; and the like. Both water soluble and water insoluble PVP polymers may be used.

In this process, the PVP powder is suspended in a suitable anhydrous organic solvent, such as a carboxylic acid ester, an alkyl ether, e.g. t-butyl methyl ether, or a hydrocarbon, e.g. cyclohexane. Preferably, however, an alkyl or cycloalkyl ester of a saturated aliphatic carboxylic acid is used, as for example, ethyl acetate, propyl acetate, isopropyl acetate, butyl acetate and ethyl propionate. The PVP suspension in ethyl acetate, for example, then is cooled, preferably to about 0°C., at which temperature precipitation f the desired complex as a fine powd r may suitably occur.

An anhydrous H_2O_2 solution in an anhydrous organic solvent, preferably the same carboxylic acid ester used to form the PVP suspension, then is prepared according to the process of U.S. 4,564,514. In this step, an aqueous H_2O_2 solution (e.g. a 50% solution) is treated with the ester and then subjected to azeotropic distillation at a predetermined low pressure, e.g. at 200 mm Hg and 55°C. The resultant product is an anhydrous H_2O_2 solution in the ester having a H_2O_2 concentration in the range of about 20 to 50% H_2O_2.

Thereafter the thus-prepared anhydrous H_2O_2 solution is slowly added to the cooled PVP suspension in an anhydrous solvent in an amount corresponding to the desired molar ratio of PVP and H_2O_2. Preferably, however, a small excess of the H_2O_2 solution over the desired stoichiometric ratio is used. For example, to prepare a PVP-H_2O_2 complex with a 1:1 molar ratio, about 111 g. PVP and 100 g. of a 42% H_2O_2 and 300 ml of anhydrous solvent is used, providing a small excess, e.g. about 5%, over the required stoichiometric amount of 34 g. H_2O_2. This excess H_2O_2 is recoverable from the mother liquor.

Upon mixing the PVP and H_2O_2, a fine white powder is obtained which is filtered and dried at about 40-50°C. in vacuo to remove residual solvent. The product is a stable, anhydrous complex in the form of a uniform, free-flowing, fine white powder having a H_2O_2 content between about 13% (2:1 molar ratio) and 23% H_2O_2 (1:1 molar ratio). The water content of the product generally is equal to or less than the amount present in the PVP starting material, and usually is less than 1%, preferably about 0.5%.

An alternative process for preparing the substantially anhydrous complexes of the invention uses a water-insoluble PVP polymeric starting material which is available commercially as a solid of varying molecular

w ight and water content. A suitable water-insoluble PVP polymer is Crospovidone, sold by GAF Chemicals Corp., which contains about 4% water. These PVP powders preferably are dried at about 105°C. in vacuo for about 2 hours to reduce the water content to less than about 1%.

The dried PVP powders then are suspended at about 5-10°C. under agitation in a substantial quantity of an anhydrous organic solvent, such as a carboxylic acid ester, a dialkyl ether, e.g. t-butyl methyl ether, or a hydrocarbon e.g. hexane or cyclohexane. Preferably an alkyl or cycloalkyl ester of a saturated aliphatic carboxylic acid is used, as for example, ethyl acetate, propyl acetate, isopropyl acetate, butyl acetate and ethyl propionate. Ethyl acetate is preferred.

A 70-85% aqueous H_2O_2 solution then is added to the cooled PVP suspension under continued agitation during a period of about 30 minutes to about 1 hour. The amounts of PVP starting material and H_2O_2 solution used correspond to the desired molar ratio of PVP and H_2O_2 in the complex. Preferably, however, a small excess of the H_2O_2 solution over the desired stoichiometric ratio is used. This excess H_2O_2 is recoverable from the mother liquor.

Upon mixing the PVP and H_2O_2, a uniform, free-flowing, fine, white powder precipitate is obtained which is filtered and dried at about 40-50°C. in vacuo to remove residual solvent and water. The product is a stable, anhydrous complex in the form of a uniform, free-flowing, fine, white powder having a H_2O_2 content between about 18 and 22% H_2O_2. The water content of the product generally is about 2% or less, and usually can be dried to less than about 1%.

Continued drying under these low temperature and vacuum conditions reduces the final water content in the complex to a substantially anhydrous powder with no loss of H_2O_2.

EXAMPLE 1

Preparation of Substantially Anhydrous 1:1 PVP-H_2O_2 Complex

PVP K-30 (GAF Corp.) (4.5% water), 111 g., was suspended in 200 ml. of anhydrous ethyl acetate (0.01% H_2O), and the suspension was cooled to 0°C. An anhydrous hydrogen peroxide solution in ethyl acetate was prepared by treating 200 g. of 50% aqueous hydrogen peroxide with 6 l. of ethyl acetate and azeotroping in a rotary evaporator to remove 100 g. of water. A 42.7% H_2O_2 solution in anhydrous ethyl acetate was obtained. Then 100 g. of this solution was added slowly over a period of about 1-1/2 hours to the PVP suspension. A fine white precipitate formed which was filtered and dried in vacuo. The resultant water soluble complex contained 23.4% by weight H_2O_2 and 0.5% by weight water, upon drying at 50°C. in vacuo for 2 hours.

EXAMPLE 2

Preparation of Anhydrous 2:1 PVP-H_2O_2 Complex

The process of Example 1 was followed using 50 g. of the H_2O_2 solution in anhydrous ethyl acetate. The resultant complex contained 13.2% H_2O_2 and 0.5% water.

EXAMPLE 3

200 g. of PVP-CI (K-30) was suspended in 300 g. of anhydrous ethyl acetate. Then H_2O_2, 424 g., 19.6% H_2O_2 and 0.84% H_2O was added slowly to the cooled (5°C.) suspension f PVP/ethyl acetate. The addition required 45 minutes. The suspension then was stirred for

another 45 minutes, filtered, and washed with anhydrous ethyl acetate. The fine powder was dried at 40-50°C. for 2 hours under vacuum to recover ethyl acetate. The yield was 258.8 g. of water soluble PVP-H_2O_2 containing 23.1% H_2O_2 and 0.4% H_2O as a free flowing white powder. The mother liquor of ethyl acetate, 485 g. contained 4.51% H_2O_2.

EXAMPLE 4

35 g. of crospovidone was suspended in 100 ml. of anhydrous ethyl acetate. Then H_2O_2, 27.5 g. as a 42.7% H_2O_2 solution was added with cooling at 5-10°C. The mixture was stirred for 1 hour. The precipitated complex was filtered to provide 46.1 g. of a water insoluble PVP-H_2O_2 complex containing 24.9% H_2O_2, after drying at 40-50°C. for 2 hours.

COMPARATIVE EXAMPLE

Preparation of Aqueous PVP-H_2O_2 Complex According to U.S. 3,480,557

6 g. of PVP-CI (K-30) (GAF Corp.) (4.5% water) was dissolved in 50 ml. of methanol. Then 7 g. of a solution of H_2O_2 in water (50%) was added, followed by heating at 45°C. for 2 hours, and evaporation of methanol for 12 hours. A gummy, amorphous residue was obtained which contained 12.92% H_2O_2 and 5% H_2O.

EXAMPLE 5

Stability of Anhydrous Complex of Example 1

After 43 days at 60°C. the complex lost only 15% of its H_2O_2 activity, which shows excellent stability toward decomposition. At room temperature, decomposition was only 1.5% after 60 days.

EXAMPLE 6

Preparation of Free-Flowing, Fine, White Powders of PVP-H_2O_2 Complex

PVP-CI (K-30) (GAF Corporation) (4.5% water) was dried at 105°C. in vacuo for 2 hours until it contained only 1.1% water. 160 g. of the dried, water-insoluble PVP was suspended in 450 g. of anhydrous ethyl acetate (0.01% water), and the suspension was cooled to 5°-10°C. while agitating the suspension. Then 55 ml. of 70% hydrogen peroxide solution in water (71 g. H_2O_2) was added slowly over a period of 35 minutes to the agitated suspension keeping the temperature at 5°-10°C. A fine, white precipitate was formed which was filtered to yield 312 g. of a wet product which was dried at 40°-50°C. in vacuo for 4 hours. 200 g. of a free-flowing fine, white powder was obtained which contained 19.5% H_2O_2 and 2.9% water. Further drying under the same conditions for an additional 6 hours reduced the water content to 0.5% while maintaining the H_2O_2 content at 18.5% and without affecting the physical properties of the powder.

In the drying step above, 77.9 g. of mostly ethyl acetate was collected in the vacuum trap which also contained 0.2% H_2O_2 and 3.78% water in the upper layer and 8.0 g. of mostly water (92%) with 0.63% H_2O_2.

The filtrate (363 g.) obtained above contained 2.75% H_2O_2 and 1.54% H_2O, the rest being ethyl acetate, which was recycled as described in Example 2 below.

EXAMPLE 7

The procedure of Example 6 is followed using PVP-CI 160 g.; ethylacetate 450 g.; and 85% H_2O_2 56 g. 197 g. of a PVP-H_2O_2 complex with 19.2% H_2O_2 containing 1.56% H_2O is obtained. Further drying at 40-50°C. in vacuo will reduce the water content to 0.5% H_2O.

EXAMPLE 8

Preparation of Free-Flowing, Fine, White Powders of PVP-H_2O Complex by Recycling the Filtrate of Example 1

To the filtrate from Example 6, 363 g., was added 90 g. of fresh, anhydrous ethyl acetate followed by cooling to 5°-10°C. Then 170 g. of dried PVP-CI was added at once whereupon the exothermic reaction increased the temperature to 12°C. The suspension was cooled to 5°C. with an ice-water bath. Then 58 g. of a 70% H_2O_2 solution was added over a period of 2 hours with good agitation. a fine, white precipitate was formed and filtered to provide 320 g. of a wet cake which was dried at 40°-50°C. under vacuo for 4 hours to yield 202 g. of a free-flowing, fine, white powder containing 18.9% H_2O_2 and 3.1% H_2O. Further drying under the same conditions for an additional 6 hours lowered the water content to 0.6%, and the H_2O_2 content to 18.3%, without affecting the physical characteristics of the powder.

The filtrate weighed 358 g., and was mostly ethyl acetate with 2.58% H_2O_2 and 1.49% water.

COMPARATIVE EXAMPLE 2

Preparation of Aqueous PVP-H_2O_2 Complex according to U.S. 3,480,557

To 6 g. of PVP-CI (K-30) (GAF Corporation) (4.5% water) was dissolved in 50 ml. of methanol was added 7 g. of a solution of H_2O_2 in water (50%), followed by heating at 45°C. for 2 hours, and evaporation of methanol for 12 hours. The gummy, amorphous residue contained 12.92% H_2O_2 and 5% H_2O.

EXAMPLE 9

Stability of Anhydrous Complex of Example 6

After 43 days at 60°C. the complex lost only 15% of its H_2O_2 activity, which shows excellent stability toward decomposition. At room temperature, decomposition was only 1.5% after 60 days.

EXAMPLE 10

Stability of Aqueous Solutions of Anhydrous Complex of Example 6

An aqueous solution of the complex of Example 6 containing 3.75% H_2O was heated at 58°C. for 96 hours. At the end of this period, the solution analyzed for 2.75% H_2O, which indicated excellent stability for aqueous solutions of the complex of the invention.

COMPARATIVE EXAMPLE 3

Stability of Aqueous Solutions of (a) Urea/H_2O_2 and (b) H_2O_2

(a) Under the same conditions as in Example 10, a urea/H_2O_2 solution, after only 36 hours, was reduced in H_2O_2 content from 3.5% to 0.6% H_2O_2. (b) An H_2O_2 solution itself lost all of its 3.0% H_2O_2 content after 36 hours.

Antimicrobial formulations of the complexes of the invention are prepared using a microbiocidal amount of the substantially anhydrous PVP-H_2O_2 complex, and an acceptable diluent and/or other active and inactive ingredients in the form of a suspension, solution, dispersion gel, powder, paste, suppository, aerosol, ointment, tablet, etc. The formulation may also be impregnated into or applied onto a suitable support, such as a gauze, cotton swab, sponge, etc. Generally, the complex will be activated by water present on the surface containing the microbes, the water functioning to release the active H_2O_2 from the complex.

FORMULATION 1

VAGINAL SUPPOSITORY

Ingredient	Percent	Wt.
Anhydrous PVP-H_2O_2 (23.1%)(Ex.1)	14.29	0.3000
Nonoxynol-9	4.76	0.1000
Amphoteric-19	1.71	0.0360
Povidone	4.29	0.0900
Citric acid, anhydrous	1.93	0.0405
Sodium bicarbonate	3.21	0.0675
Polyethylene glycol 1000	66.43	1.3950
Polyethylene glycol 1540	3.38	0.0710
	100.00%	2.100

The suppository dissolves completely in about 1 ml of water in about 10 minutes at a temperature of about 37°C. Upon contact with water, a slight development of foam starts with simultaneous dissolution of the suppository. The foam development increases constantly until the dissolution is complete. The foam which forms has fine pores, is even and remains as such over an extended period of time. The nonoxynol-9 is a spermaticide, and the amphoteric-19 and PVP-peroxide are microbiocides.

FORMULATION 2

EFFERVESCENT MOUTHWASH TABLET

Ingredient	Percent	Wt. (grams)
Anhydrous PVP-H_2O_2 (23.1%) (Ex.1)	27.29	0.122
Sodium bicarbonate (granular)	22.4	0.100
Sodium carbonate, anhydrous	2.24	0.010
Citric acid, anhydrous (granular)	44.74	0.200
Aminoacetic acid	1.79	0.008
Flavorants (spray dried)	1.11	0.005
Color	0.22	0.001
Sodium benzoate (fine powder)	0.22	0.001
	100%	447 mg.

The tablets are compressed with 3/4-in. diameter, flat-faced, bevel-edge tooling. The tablet ingredients, other than the anhydrous PVP-peroxide complex, are mixed, lightly dampened, and granulated. To the slightly dampened granules the anhydrous PVP-peroxide complex is added, and the well-mixed, slightly moist ingredients are compressed, then immediately thereafter placed in a 70°C. forced draft oven for 1 hour to drive off any residual water. The cooled tablets are immediately packaged in air tight aluminum foil pouches.

The tablets are added to 60 cc (2 oz.) of water for use as an effervescent mouthwash and gargle.

FORMULATION 3

NON-AQUEOUS OINTMENT

Ingredient	Percent	Wt. (g.)
Anhydrous PVP-H_2O_2 (23%) (Ex.1)	15	150
Sorbitan Monopalmitate (Span® 40-Atlas)	1	10
Polyethylene Glycol 400 Monostearate	14	140
Polyethylene Glycol 400	35	350
Polyethylene Glycol 4,000	35	350
	100%	1,000 g.

The polyethylene glycols and the sorbitan monopalmitate are warmed on a water bath to 70°C. and the complex is added to the well-stirred molten mass. Stirring is continued until the ointment is well-solidified.

FORMULATION 4

ANTIBACTERIAL LIPSTICK

Ingredient	Percent	Wt. (g.)
Anhydrous PVP-H_2O_2 (23%) (Ex. 1)	15	0.30
Polyethylene glycol 1000	17	0.34
Polyethylene glycol 4000	68	1.36
	100%	2.00 g.

The formulation is prepared as in 3 above.

FORMULATION 5

POLYETHYLENE GLYCOL-CONTAINING OINTMENT

Ingredient	Percent	Wt.(g.)
Anhydrous PVP-H_2O_2 (23%) (Ex. 1)	15.17	21
Sodium Carbonate	5.06	7
Polyethylene Glycol 4000	36.13	50
Polyethylene Glycol 400	43.64	60.4
	100%	138.4 g.

Heat the polyethylene glycol 4000 and 400 with constant stirring on a water bath at 65°C. Slowly add the micronized anhydrous sodium carbonate and PVP-H_2O_2 complex with constant stirring. Cool until the mass is well mixed and congealed.

FORMULATION 6

ANHYDROUS TOOTHPASTE

No.	Phase	Ingredient	% by Wt.
1	E	Anhydrous PVP-Hydrogen Peroxide (23%) (Ex. 1)	15
2	A	Glycerin	10
3	A	Xanthum Gum	0.25
4	B	Polyethylene Glycol 400	47
5	C	Thixcin	0.25
6	C	Povidone K-90	0.5
7	D	Monosodium Phosphate	0.7
8	D	Trisodium Phosphate	1.25
9	D	Sodium Saccharin	0.2
10	D	Sodium Fluoride	0.25
11	D	Abrasive Silica	15
12	D	Thickening Silica	6.6
13	D	Titaniunm Dioxide	0.5
14	D	Sodium Lauryl Sulfate	1.2
15	E	Flavor Oil	1.2
16	E	Pigment	0.1
			100.0%

All D items in formula above should be micropulverized and blended. Sprinkle the xanthum gum into glycerin with constant agitation until uniform (Phase A). Add the polyethylene glycol 400 (Phase B) to Phase A with continued agitation. Sprinkle in Povidone K-90 until uniform and with constant stirring add the well mixed micronized ingredients of Phase D. Seal unit with cover and apply 28 or more inches of vacuum for 30-45 minutes with continuous agitation. Add all ingredients of phase E, starting with the hydrogen peroxide complex (it m 1), under continued agitation and mix until uniform. Mix under vacuum (28 inches or more) f r 5 additional minutes.

FORMULATION 7

TOOTH POWDER

Ingredient	Percent	Wt. (grams)
Anhydrous PVP-H_2O_2 (23%) (Ex. 1)	15.0	15.0
Calcium Sulfate	52.35	52.35
Dicalcium Phosphate	27.0	27.0
Povidone K-90	1.5	1.5
Sodium Saccharin	0.15	0.15
Sodium Lauryl Sulfate	3.0	3.0
Flavor	1.0	1.0
	100%	100 grams

FORMULATION 8

MEDICATED BANDAGE

Ingredient	Percent	Wt.(g.)
Anhydrous PVP-H_2O_2 (23%) (Ex. 1)	14.3	100
Povidone K-90	85.7	600
	100%	700 g.

Blend micronized powders of the above two ingredients until homogeneous. Add ethyl alcohol to the well blended powder until a thick homogeneous paste is achieved. Lay a homogeneous layer of 700 mg plus the ethyl alcohol used for dispersion on 1 sq. inch of bandage. Place the coated bandage material under vacuum and heat until the ethyl alcohol is completely evaporated. The resultant mixture of the H_2O_2 complex and povidone K-90, evenly spread on 1 square inch of bandage will yield about 3% of available H_2O_2 from the solid p vidon mixture.

If substantive microbicide activity is desired, 0.1% of cetyl pyridinium chloride can be mixed into the above blend before evaporation of the ethyl alcohol.

FORMULATION 9

EAR DROPS SOLUTION

Ingredient	Percent	Wt.(g.)
Anhydrous PVP-H_2O_2 (23%) (Ex. 1)	6.5	6.5
Anhydrous glycerol	93.5	93.5
	100%	100g.

FORMULATION 10

SOFT LENS DISINFECTION TABLET

Ingredient	Percent	Wt.(g.)
Anhydrous PVP-H_2O_2 (23%) (Ex. 1)	81.5	1.50
Sodium bicarbonate (granular)	5.4	0.10
Sodium carbonate, anhydrous	0.6	0.01
Citric acid, anhydrous granular	10.8	0.20
Sodium benzoate (fine powder)	1.7	0.03
	100%	1.84 g.

The tablet ingredients, other than the anhydrous PVP-H_2O_2 and sodium benzoate are mixed, lightly dampened to form a damp granule. To the slightly dampened granules the povidone peroxide and sodium benzoate are added so that granules with a damp feel are compressed using 1-1/4" flat-faced, bevel-edge punches. Immediately

after compression the damp tablets are placed in a 70°C. forced draft oven for 1 hour to drive off any residual water. The cooled tablets are immediately packaged in air-tight aluminum foil pouches.

FORMULATION 11

MEDICATED POWDER

Ingredient	A	B	C
PVP K-30-H_2O_2 (6.47%) (Soluble PVP)	10	50	60
PVP-Crospovidone-H_2O_2 (23.67%) (Insoluble PVP)	10	1	5
Talc	60	45	30
PVP K-30	10	--	--
Polyplasdone® XL10	10	4	5
H_2O_2 Activity	3%	3.5%	5.0%

The above powders were mixed together to provide the desired composition.

FORMULATION 12

WOUND DRESSING

Ingredient	Percent	Wt. (g.)
Anhydrous PVP-H_2O_2 (22.8% H_2O_2)	10	10
Absolute Ethanol	90	90
	100%	100 g.

A 1% H_2O_2 solution of the above composition is applied to a wound. A film is formed which is effective to disinfect the wound.

FORMULATION 13

COLD WATER LAUNDRY TABLET

Ingredient	Percent	Wt. (g.)
PVP-H_2O_2 (23%) (Ex. 1)	81.5	1.50
Sodium benzoate (fine powder)	1.64	0.03
	100%	1.84 g.

These anhydrous PVP-H_2O_2 tablets are an effective cold water bleach-disinfectant for cleaning clothes, etc. In use, the PVP portion of the complex can chelate with inorganic ions (e.g. Ca^{++}, Mg^{++}) in the water to reduce water hardness. It can also provide laundry detergents with the properties of antiredeposition or suspension of dirt, anti-dye transfer, along with its bleaching and disinfectant action.

FORMULATION 14

WATER DISINFECTANT TABLET

Ingredient	Percent	Wt. (g.)
Sodium bicarbonate	6.3	0.10
Sodium carbonate, anhydrous	0.6	0.01
Citric Acid, anhydrous granules	12.6	0.20
Povidone-H_2O_2 (20%)	78.6	1.25
S dium benzoate (fine powder)	1.9	0.03
	100.0%	1.59 g.

This tablet should be dissolved in one quart of water and allowed to remain for 5 minutes after the tablet is dissolved before the water is ready to drink. To prepare the tablet, follow the same directions as given in Formulation 10 except use a 1 inch flat-faced, bevel-edge punch.

The above formulations and applications illustrate methods of reducing the bacterial content of surfaces using the anhydrous PVP-H_2O_2 complex of the invention.

WHAT IS CLAIMED IS:

1. A stable complex of PVP and H_2O_2 in a molar ratio of between about 2:1 and about 1:1, respectively, which is obtained as a uniform free-flowing, fine, white powder by direct reaction between suspended PVP and H_2O_2 in substantially the molar ratio predetermined for the complex.

2. A complex according to claim 1 wherein the complex contains essentially little or no water or free hydrogen peroxide therein.

3. A process of preparing a stable, uniform free-flowing powder complex of PVP and H_2O_2 which comprising suspending PVP powders in an anhydrous medium and reacting H_2O_2 therewith.

4. A process according to claim 2 wherein the H_2O_2 is reacted in substantially the same molar ratio as desired in the complex.

5. A process according to claim 3 in which PVP is suspended in anhydrous ethyl acetate.

6. A suspension process for preparing uniform, free-flowing fine, white powders of a substantially anhydrous complex of PVP and H_2O_2 having an H_2O_2 content between about 18 and about 22% H_2O which comprises:

(a) forming a suspension of water-insoluble PVP containing less than about 1% water in an anhydrous organic solvent,

(b) slowly adding a predetermined amount relative to the PVP of an aqueous H_2O_2 solution containing about 70 to about 85% by weight H_2O_2, at a temperature of about 0°-10°C. under agitation to precipitate a PVP-H_2O_2 complex in the form of a uniform, free-flowing, fine, white powder,

(c) filtering, and

(d) drying the wet precipitate to form the desired powders.

7. A suspension process according to claim 6 wherein said organic solvent is anhydrous ethyl acetate.

8. A process according to claim 6 wherein the filtrate is recycled for use in step (a).

9. A process according to claim 6 wherein drying is carried out at about 50°-60°C. in vacuo.

10. A method for reducing the microbial content of surfaces which comprises contacting said surface with a microbiocidal amount of a substantially anhydrous complex of PVP and H_2O_2 in the form of a free-flowing powder having an H_2O_2 content of about 3 to 24% by weight, wherein said complex is present in a formulation in an amount of about 0.1 to 15% by weight.

11. A method according to claim 10 wherein said complex is present on a support.

12. A method according to claim 11 wherein said support is a gauze, cotton swab or sponge.

13. A method according to claim 10 wherein said complex is present in a non-aqueous formulation.

14. A method according to claim 10 wherein said surface comes into contact with living tissue.

15. A formulation for reducing the microbial content of surfaces which include a microbiocidal amount of an anhydrous PVP and H_2O_2 complex, having an H_2O_2 content of about 3 to 24% by weight.

16. A method according to claim 1 further characterized in that said surface is contacted in the presence f water.

17. A formulation according to claim 16 wherein the complex has a molar ratio of PVP and H_2O_2 between about 2:1 and about 1:1.

18. A formulation according to claim 16 which also includes one or more of an acceptable diluent, and an active or inactive ingredient.

19. A formulation according to claim 16 which is in the form of a suspension, solution, suppository, gel, powder, paste, ointment, or tablet, optionally, on a support.

20. A formulation according to claim 16 which is a non-aqueous composition.

21. A formulation according to claim 16 which is a vaginal suppository, an effervescent mouthwash, a non-aqueous ointment, a polyethylene glycol-containing ointment, an anhydrous toothpaste, a tooth powder, a medicated bandage, an ear drop solution, a soft lens disinfectant tablet, a medicated powder, a wound dressing, a cold water laundry tablet, or a water disinfectant tablet.

INTERNATIONAL SEARCH REPORT

International Application [1] PCT/US90/05846

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC

INT. CL. (5): A61K 33/00
U.S. CL. 424/80

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
U.S.	424/80, 661, 401, 43, 53, 433, 466

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category *	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
X	US, A, 3,480,557 (SHIRAEFF) 25 NOVEMBER 1969; See column 4, paragraph 1.	1-21
X	US, A, 3,376,110 (SHIRAEFF) 02 APRIL 1968 See column 4 through column 6.	1-21
Y	US, A, 4,801,460 (GOERTZ) 31 JANUARY 1989 See entire document.	1-21

* Special categories of cited documents: [10]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
04 JANUARY 1991	13 FEB 1991
International Searching Authority	**Signature of Authorized Officer**
ISA/US	Peter Kulkosky

Form PCT/ISA/210 (second sheet) (Rev.11-87)